Recd 12/16/69

SUMMER COLLOQUIUM IN THEORETICAL BIOLOGY
Fort Collins, Colorado - 1969

N.A.S.A. -- A.I.B.S.

Director, J. F. Danielli

NGR-33-015-016

Center for Theoretical Biology
State University of New York at Buffalo
4248 Ridge Lea Road
Amherst, 14226 New York

Report prepared by Marian May

03

CONTENTS

ORGANIZATION OF THE COLLOQUIUM

The faculty members were chosen after the decision had been made on the area of study for the Colloquium. Brian Goodwin was asked to head the group working on Time-dependent Variations in Cells. Ernest Pollard, Paul Scheie and J. F. Danielli would lead the group on Intracellular Relationships and Cell Theory. Robert Rosen and Martynas Ycas headed the group working on Pattern Generation and Morphogenesis. Howard Pattee, Luigi Bianchi and Jon Hamann were asked to head the group on Self-reproducing Automata and Relational Systems and Cell Theory. N. Leibovic led the Information Processing by Cell Assembly group. At first, six working parties had been suggested, but due to the shortage of funds, Dr. Pattee's group and Dr. Bianchi and Mr. Hamann's group were amalgamated.

When the faculty had accepted the invitation to head the groups, the Colloquium was advertised in the usual ways. This resulted in receipt of around 100 applications. The faculty met with the Director to consider these applications after complete files and references had been obtained for each one. Applicants were assessed according to their suitability to fit into the working parties and twenty were selected as being best qualified to work productively in the various groups. A back-up list of 33 applications were placed in order of suitability for various working parties and were invited after the first group had indicated whether they would be able to attend or not. Since funds were extremly short due to reduction in available funds and to large increases in costs, each successful applicant was asked to obtain funds, if possible, from other sources. Subsequent to obtaining this information, other suitable applicants were invited as funds became available. In all thirty applicants attended.

A general meeting was held at the start of the Colloquium to communicate relevant information to the group and to answer queries. The faculty met on the average once a week to discuss progress in their groups and to arrange lectures for the next week. Formal lectures were given two or three days a week at 8:30 AM, followed by discussion, after which parties adjourned to their own meeting rooms. Each working party arranged their own program. They took the general form of discussion groups in the morning and evening with study and preparation of reports in the afternoon. The entire Colloquium was maintained at an informal level, allowing full freedom of movement between groups and the spontaneous formation of interest groups.

The time period of the Colloquium was considered to be most suitable for the initiation, discussion and completion of the working party studies. A longer time would have been too heavy a load to carry at this pace.

The last few days of the Colloquium were devoted to the report - back sessions of working party accomplishments. Members rather than faculty gave these talks and it was thought to be a valuable experience by the working party members. The Colloquium resulted in the output of some new and original work. About twenty papers arising from the Colloquium will be published in a special issue of the Journal of Theoretical Biology.

The Colloquium as a whole was considered at the final faculty meeting. There was common agreement that this was a very successful meeting, though there were a small number of individuals who did not participate adequately in the program.

The formal lectures were agreed to have been a success this year. They were flexible and evolved as the conference progressed.

A mixture of experimentalists (with theoretical leanings) and theoreticians should be encouraged for these types of meetings.

Work would continue on many of the projects studied at the meeting and a number of new projects were evolved, e.g. it was thought desirable to have a study made of reassembly of egg cells from components.

It was agreed that a further Colloquium should be held in about three years time. A further meeting sooner than this would not be justified since new ideas would not have had time to mature.

WORKING PARTIES

Subject, faculty,participants

Reports

GENERAL LECTURES

Time	Title	Speaker
July 16 8:30 AM	Synthesis of E. Coli	E. Pollard
July 17 8:30 AM	Temporal Spatial Mappings for Positional Information in Embryos	B. Goodwin
July 22 8:30 AM	Temporal Spatial Mappings (con't.)	B. Goodwin
July 23 8:30 AM	Development of Order in Random Switching Networks	S. Kaufman
July 24 8:30 AM	Ordering Principles in Continuous and Discrete Systems	H. Pattee
July 29 8:30 AM	Metamorphosis of Fruit Flies, Spontaneous Diurnal Rhythm	A. Winfree
July 29 7:00 PM	Film on Embryology	B. Goodwin
July 30 8:30 AM	Activity of single cells in the Nervous System	K.N. Leibovic
July 31 8:30 AM	Synthesis of Cells	J.F.Danielli K. Jeon
August 5 8:30 AM	Protein Structure	D. Warner
August 6 8:30 AM	Discussion on Minimal Membranes	J.F.Danielli
August 7 8:30 AM	Relational Systems	J. Hamann L. Bianchi
August 8 1:30 PM	Session on Muscle	D. Shear
August 11 1:30 PM	Session on Aging	J.F.Danielli
August 12 August 13 August 14 8:30 AM	Report-back Sessions (see program page 7)	

WORKING PARTY I - Time-dependent Variations in Cells

Faculty: Dr. B. Goodwin, University of Sussex, England

Participants:

Dr. S. Kaufman, University of Chicago, Illinois
Dr. A. Winfree, University of Chicago, Illinois
Dr. E. Manougian, University of California, Berkeley
Mr. W. Woolley, University of Maryland, College Pk.
Dr. D. Mantik, Hansen Laboratories, University of Stanford, California

WORKING PARTY II - Intracellular Relationships and Cell Theory

Faculty: Dr. J. F. Danielli, SUNY at Buffalo, N.Y.
Dr. E. A. Pollard, Pennsylvania State University, University Park, Penna.
Dr. Paul Scheie, Pennsylvania State University, University Park, Penna.

Participants:

Miss K. Moelling, University of California, Berkeley
Dr. K. Jeon, SUNY at Buffalo, N.Y.
Mrs. V. Jordan, University of Maine, Orono
Dr. N. Goel (transfered to III) University of Rochester, N.Y.
Dr. M. May, SUNY at Buffalo, N.Y.

WORKING PARTY III - Pattern Generation and Morphogenesis

Faculty: Dr. R. Rosen, SUNY at Buffalo, N.Y.
Dr. M. Ycas, Upstate Medical Center, Syracuse, N.Y.

Participants:

Dr. L. Demetrius, University of California, Berkeley
Dr. H. Martinez, University of California, San Francisco
Dr. R. Campbell, University of California, Irvine
Mr. R. Schwartz, Stanford University, California
Dr. R. Gordon, SUNY at Buffalo, N.Y.

WORKING PARTY IV - Self-reproducing Automata, Relational Systems and Cell 1 Theory

Faculty: Dr. H. Pattee, Stanford University, California
Dr. L. Bianchi, SUNY at Buffalo, N.Y.
Mr. J. Hamann, SUNY at Buffalo, N.Y.

Participants:

Dr. M. Conrad, Stanford University, California
Dr. R. Moore, SUNY at Plattsburg, N.Y.
Dr. M. Pincus, Brooklyn Polytechnic Institute, N.Y.
Dr. D. Shear, University of Georgia, Athens
Dr. P. Bright, University of Texas, SW, Dallas
Dr. S. Stivala, Stevens Institute of Technology, Hoboken, New Jersey

WORKING PARTY V - Information Processing by Cell Assembly

Faculty: Dr. K. N. Leibovic, SUNY at Buffalo, N.Y.

Participants:

Dr. E. Balslev, SUNY at Buffalo, N.Y.
Mr. T. Mathieson, SUNY at Buffalo, N.Y.
Dr. K. Reid, University of Louisville, Kentucky
Dr. O. Sittler, University of Eastern New Mexico, Portales
Mr. V. Jayanthinathan, SUNY at Buffalo, N.Y.
Mr. H. Geller, Case Western Reserve University, Cleveland, Ohio
Mr. G. Pertile, Syracuse University, N.Y.
Mr. F. Young, Syracuse University, N.Y.
Dr. C. Torda, NYU Medical College, N.Y.
Mr. P. Cull, University of Chicago, Illinois

PROGRAM
Report-back Sessions

Wednesday, August 13th

Group I Chairman Ed Manougian

8:30 AM	S. Kauffman - Genetic variability, phenotypic stability and neoplasia; or flak and fluff.
9:15	W. Woolley - A model of homeostatic control system deriving from a Hamiltonian
10:00	Coffee Break
10:10	S. Newman - An integrative principle for physics and biology
10:55	Winfree's conjecture

Group II Chairman J. F. Danielli

1:30 PM	Paul Scheie - Limits of existence of cells
2:15	Karin Moelling - Spatial relationship between DNA, RNA and Ribosomes in *E. coli*
3:00	Marian May - Hypotheses of steroid action
7:00	Consideration on Cells for Mars (a) Virginia Jordan - Review of isoprene biochemistry
7:45	(b) J.F. Danielli - Hypothetical isoprene based macromolecules

Chairman - M. Ycas

8:30 PM	Special Presentation - J. F. Danielli Application of Maxwell's theories of cells

Thursday, August 14th

Group III Chairman M. Ycas

8:30 AM	R. Rosen - Introductory statements
8:40	M. Martinez - Absolute Maxima
9:00	N. Goel - Absolute Maxima
9:40	Coffee break
10:15	R. Campbell - Local Maxima
10:35	M. Ycas - Onions

Thursday, August 14th (con't)

Group IV Chairman J. Hamann

11:00 AM	J. Hamann - Random Control
11:30	P. Bright - Evolution of life vs Newtonian mechanics
1:30 PM	R. Conrad - Ecological stability and parallel processing
2:15	M. Pincus - A stochastic optimization procedure
3:00	D. Shear - Examination of the properties of stability (a specific case)

Group V Chairman K. N. Leibovic

7:00 PM	K. N. Leibovic - Two problems on information processing
7:30	E. Balslev - Mathematical investigations of binocular space perception
8:15	T. Mathieson - Experimental work on binocular space perception
8:45	K. Reid - Quantitative Analyses of experimental data on visual adaptation
9:25	H. Geller - Analysis and retinal organization

TIME DEPENDENT VARIATION IN CELLS

a) Proposed program - pre-circulated

I would like to consider the questions and topics listed below. The scope of these problems is broad, and the reading lists are a thin covering of the ground. Any papers that you think are relevant to these questions will be very useful to have at the Colloquium.

1) Temporal order: the cell cycle.

1. What dynamic behaviour is to be expected in self-reproducing systems?

a) Dynamical characterization of self-reproduction: a self-reproducing system returns to the neighbourhood of its initial state, defined in terms of intensive variables, after a finite period of time.

2. What kind of stability do self-reproducing systems have?

3. How does one introduce statistical variation into a dynamical system with asymptotic stability? Add a stochastic variable to the dynamics? Construct a statistical mechanics?

a) Methods of constructing Hamiltonians for dynamical systems with attractor sets (asymptotic stability).

4. A dynamical theory of the cell cycle.

READING LIST

M. Arbib (1969). Self-reproducing automata - some implications for theoretical biology in "Towards a Theoretical Biology", Vol. II. Edinburgh University Press, p. 204.

P. Fong (1968). Phenomenological Theory of Life. J. Theoret. Biology, 21, 133.

B. Goodwin (1969). Growth Dynamics and Cell Synchronization in "Microbial Growth", p. 223. Cambridge University Press. S.G.M. Symposium 19.

S. Kauffman (1969) Metabolic stability and epigenesis in redundancy constructed genetic nets. J. Theoret. Biol., 22, 437.

R. Pritchard et al (1969). Control of DNA Synthesis in Bacteria in "Microbial Growth", S.G.M. Symposium 19, 263.

A. Winfree (1969). The temporal morphology of a biological clock in A.A.A.S. Symposium, "Some Mathematical Problems in Biology".

2) Temporal and Spatial Order: epigenesis.

1. Given that cells are self-reproducing systems, temporally differentiated and hence with periodicities in variables defining their state, how could spatial order arise in aggregates of interacting cells?

2. A periodic wave-propagation model of epigenesis: spatial order from temporal order via synchronization and phase-shifting.

a) Experimental and theoretical implications of this theory.

b) Analysis of embryonic fields and pattern formation in hydra, early amphibian development, and the retinal-tectal projection in the amphibian visual system.

c) Evidence for the theory from experiments on regeneration in *Hydra littoralis*.

READING LIST

J. T. Bonner (1963). "Morphogenesis", Atheneum Press.

C. H. Waddington (1956). Principles of Embryology, Chap. I., IX, X, XIV. Allen & Unwin.

G. R. Delong and A. J. Coulombre (1967). Devel. Biol. 16, 513.

R. M. Gaze, M. Jacobson, G. Szekely (1963). The retino-tectal projection in Xenopus with compound eyes. J. Physiol. 165, 484.

R. W. Sperry (1963). Chemoaffinity in the orderly growth of nerve fibre patterns and connections. P.N.A.S. 50, 703.

3) Perspective: Biological Dynamics

1. What do we want of a dynamical theory in biology? Qualitative analysis - topological properties? Quantitative prediction - dynamics and statistical dynamics?

2. Is the basic dynamic mode of activity of biological systems the limit cycle (including degenerate limit cycles, with orbital but not asymptotic stability)?

a) If so, how can we construct a comprehensive dynamical theory on this basis?

3. Is it necessary to retain a duality of description of biological process characterized roughly by the dynamics vs automata theory antinomy, analogous to the wave-particle duality of physics? Or is there a comprehensive resolution?

TIME DEPENDENT VARIATION IN CELLS

b) Report

Temporal and Spatial Organization of Biological Systems.

The main preoccupation of the group has been an attempt to deduce the dynamical behavior which characterizes complex biochemical networks under the constraints which operate in biological systems at the cellular level and above. A secondary problem is the complement of this: given particular types of dynamical behavior in cells, what spatial order is likely to emerge from aggregates of interacting cells, with particular initial and boundary conditions? So far the following analyses have been advanced:

1. Metabolic networks simulated by switching automata obeying Boolean algebra, which interact with a low order of connectivity, nearly always show cyclic behavior in their steady states. This analysis has been extended to show that metabolic networks with macromolecular control elements operating with high stoichiometry to give sharp responses will, with high probability, have low connectivity and hence will show limit cycle type behavior in the steady state. This network approach has been applied to the problem of the origin of self-replicating systems, with a demonstration that this property emerges naturally from catalytic nets with low connectivity.

2. An investigation of the dynamical consequences of certain efficiency criteria applied to chemical networks has produced evidence that optimal behavior of the network

with respect to energy utilization and product yield occur when the variables oscillate.

3. The mathematical representation of oscillating biochemical networks with stable temporal organization has been under investigation from a phenomenological point of view. One approach has been to proceed in a manner similar to that followed in the development of quantum mechanics, starting with equations of the form

$$\frac{du}{dx} = A(x)e^{i\phi(x)}$$

and with constraints on $A(x)$ and $\phi(x)$ defined by the observed behavior of biological systems. Another approach has been to study oscillatory systems with asymptotic stability which are representable in Hamiltonian form either in the original space or in a transformed space. Such systems allow of an analysis in terms of generalized statistical mechanics.

4. An investigation of a particular problem in developmental pattern formation has been carried out. A detailed model of the retinal-tested projection in the amphibian visual system in terms of the phase-shift theory, has been realized.

May 5, 1969

<u>Theoretical Biology Colloquium 1969</u>

Intracellular Relationships and Cell Theory

Dear Colleague:

Enclosed is a proposed program for our Working Party. Within a few weeks you will receive photocopies of materials listed. You are asked -

1) to propose additional topics for the Working Party

2) to contribute other materials for circulation to the group

3) to send in draft or outline manuscripts to be worked upon at Fort Collins.

Each study group will endeavor to prepare a number of completed manuscripts by the end of the meeting, which will be published as a report in a special issue of the Journal of Theoretical Biology.

Please acknowledge receipt of this letter. Further materials will reach you around May 20th and June 15th.

Yours sincerely,

Marian May for Jim Danielli

/rk

INTRACELLULAR RELATIONSHIPS AND CELL THEORY

a) Proposed program - pre-circulated

Working Method

E. C. Pollard

Three methods of working naturally develop. The first is in the general group discussion - either as forty theoreticians or as our own group. The second is in twos and threes with occasional consultants from the other groups. The third is work in the library alone. The second method is usually exciting and productive but for it to get going quite a bit of library work alone is needed and, in addition, it needs to be set in context by the first group discussion. What proves to be most helpful is a certain amount of preliminary work in the library of the home institution in the weeks prior to Fort Collins. The topics suggested act as a guide for this precharging of batteries and it is good to exert some imagination about data and mathematical methods beforehand and to bring some of the results of acting on the imagination to Fort Collins, when you come.

It will also be of help if each member will select three topics and tell us ahead. In addition he should suggest any more topics which occur to him.

What is doubtful help to us is to regard the colloquium as simply an extension of ones own exact interest. It should be an extension but capable of a deviation to join the common interest.

INTRACELLULAR RELATIONSHIPS AND CELL THEORY

a) Proposed program - pre-circulated

Circulation: Pollard*, Scheie*, Danielli*, Lin, Moelling, May, Jordan, Goel (*faculty members)

Program

Saturday, July 12 Last day for arrival of faculty members

Sunday, July 13 9AM Meeting of all faculty members
Last day for arrival of participants

Monday, July 14 8:30AM Scheie lecture - Limits of Existence of Cells

10-11:30AM Group discussion

11:30AM-7:00PM Free time

7-10:00PM Group discussion

Group discussion of the 14th will be to finalise the working program of the group, for presentation on 15th July.

Tuesday, July 15 8:30-10:30AM Lecture and discussion on hypothetical cells
1) Proposed cells for Venus (atmospheric cells) - Pollard
2) Solid state cells - Scheie
3) Proposed cells for Mars - Danielli

10:30-11:30AM
7-10:00PM Presentation of group programs to Colloquium assembly. This presentation should be the final definition of membership of Working Parites, and of relationships between Working Party programs

The following lectures will be presented, possibly on 16, 17, 18 July:

Compatibilities of Cell Components - Jeon
Diffusion and Competition Problems - Pollard
The Minimal Cell Membrane -

The following problems and topics have been proposed for discussion, and for preparation of papers:

At least three types of experiment will be discussed, with a view to defining the boundary conditions for success. These types are (i) reassembly of amoebae, (ii) reassembly of ova, (iii) insertion of chloroplasts into non-photosynthetic cells.

2. Limits of existence.

One approach to finding the minimum condition for cellular life is to stress cells to the point of irreversibility. Numerous experiments have been reported that employ one or two such stresses. A review of these with some thought to possible combinations of many stresses may permit a guess as to the minimum requirements for the transition from a non-living to a living state.

3. Solid state cell.

How much of a cell is in liquid form? Some N.M.R. experiments are currently being interpreted as showing more bound molecules than is compatible with ideas of ordinary solutions. A review of this literature is proposed together with possible implications of some solid state phenomena to our present picture of a cell.

4. Multiple valence...examples, phosphorous, sulfur.

Is this type of element essential to life? Can silicon substitute? Is the form of energy transfer associated with the change in the character of a bond essentially the only kind of energy transfer energy available to life?

5. Atmospheric cells.

The atmosphere of Venus is dense, rich and warm if not hot. Can living cells be conceived which could operate by high pressure gas kinetics in this environment? Means for flotation, for growth, and division, for capturing radiant energy and for death and decay need to be profided. Various schemes can be devised and analysed.

6. Diffusion and competition problems.

Rates of synthesis are almost diffusion limited in bacterial cells. In designing "test tube" experiments to permit life to "take Off" the rates produced may well be very small, possibly too small. In addition competition by analogous but incorrect substrates may be more damaging if the reaction vessel has no compartmentation but the living cell does.

Numbers for these processes need to be assembled and critically important experiments suggested.

7. Cells for non-aqueous liquid media.

What are appropriate structural and chemical analogs of the structural and chemical devices which have been selected for terrestrial cells, which are essentially for aqueous media?

8. What are the minimal requirements of cell membranes?

9. What more than a minimal membrane is required for morphogenesis (a) of the unicellular organism, (b) of the multicellular organism?

PLEASE NOTE: You are asked to suggest additional topics <u>now</u>.

INTRACELLULAR RELATIONSHIPS AND CELL THEORY

b) Report

The group began by discussing the limits of existence of cells. We concluded that the known range of existence for terrestrial cells far from exhausts the possibilities implicit in the terrestrial cell system. The range of known terrestrial cells is probally much more limited by range of ecological niches than by ranges in properties of material from which cells are composed.

We went on to discuss cells for Mars and Venus. One of the first conclusions was that we would like to know more of the limits of existence of a DNA genetic system e.g. limits on temperature. No work was done on this but we hope N. Goel or someone with similar interests will do so in the future.

We decided, in addition to aqueous phase cells, that gaseous cells, solid state cells, cells growing on solid surfaces and cells growing in bulk hydrocarbon media must be considered. A useful preliminary study was made of isoprene biochemistry in relation to hydrocarbon phase cells and a first study made of the possibility of constructing macromolecules and membranes from complex polyisoprenes. Membranes with some functions analogous to those of the plasma membrane of aqueous phase cells certainly can be made and it seems likely that isoprene based enzymes could be made.

An extended discussion was held on the possibility of the spontaneous assembly of E.coli given a functional genetic system and appropriate minimal biochemical systems. This discussion led into an examination of existing data on the relations of DNA, RNA, and ribosomal synthesis of proteins within the dimensions of an E.coli cell.

The alternative approach to cell synthesis, i.e., re-assembly by appropriate mechanical techniques using preformed components, was also discussed in detail. The present limitations on the success of this technique arising from incompatibility of components from different species was not felt to be likely to prevent assembly of a wide variety of cell types.

Some discussion was held of control of cell function by steroids and of the apparent inadequacy of E.coli as a model for the understanding of steroid response in mammalian systems. A review of the literature was prepared and a study made of the probable points of estrogen action.

A discussion also initiated on the minimal cell membrane. This was unproductive, perhaps due to a lack of contact between other theoretical groups with appropriate experimental systems.

PATTERN GENERATION AND MORPHOGENSIS

a) Proposed program - pre-circulated

The program of the Working Party on Pattern Generation and Morphogenesis will be the intensive study of certain selected topics belonging to the literature of "self-organization" and "self-assembly". The purpose of our work will be twofold: (a) to obtain an understanding of pattern generation as it relates to the special systems under consideration, and (b) to obtain a better insight into the nature of self-organizing systems in general.

There are three levels of biological organization in which sufficient background has been accumulated to allow a deeper study of self-organization in these systems:

a. The level of protein tertiary structure, as a function of primary structure. The prevailing hypothesis here is that the amino acid sequence of a polypeptide uniquely specifies the active folded form of the polypeptide, that this active form is a form of minimal energy, and that the transition from unfolded to folded form proceeds spontaneously. That the polypeptide is able to fold itself up correctly without the need of outside information is obviously an instance of what we refer to as self-organization.

b. The level of assembly of viable virus particles out of their components. In the simple spherical viruses, and in tobacco mosaic virus, it has been shown that typical virus particales will assemble themselves out of protein coat monomers and nucleic acids, and that therefore the information required to specify the viral structure resides completely in the inherent binding properties of the monomer units. In these viruses it is thus legitimate to speak of "self-assembly" of these particles. As in the previous case, the assembly of virus is regarded as a spontaneous passage to a least energy state, the only difference here being that we are dealing with populations of heterogeneous molecules rather than with a single molecule. In each case, however, we may note that the entity being organized is free to explore a wide variety of states (i.e. the system possesses an inherent motility), with the organized state being energetically favored.

c. The level of populations of cells. The particular systems we have in mind here, and which will be the main focus for the work of our Working Party during the summer, are those which arise in the experiments on sorting out of populations of cells taken from developing embryos. It has become clear, from the work of Holtfreter, Townes, Moscona, Steinberg, and others, that artificial aggregates of embryonic cells will organize themselves in highly specific ways, which in many cases are reminiscent of the organization of the same cells in the intact embryo. Consult the attached reading list for precise references. Our specific problem will be to study the sorting-out process, and especially to discover what light is thrown on natural morphogenesis by the behavior of these artifically produced populations.

A beginning in this direction has already been made by Steinberg. He has proposed a phenomenological model, resting on only two postulates: (a) the cells in the population are differentially adhesive, and (b) the cells are able to move around and explore alternate configurations. As he points out, these postulates make no assertions about the nature of theforces responsible for adhesion (this is why the model is phenomenological) and the conclusions will hold for any population of motile, differentially adhesive units (such as for the individual molecules in a mixture of two or more immicible liquids). Steinberg's model, and the experimental work he has done to corroborate this model, are fully reported on in Steinberg's papers, and I would urge all members of the Working Party to become familiar with Steinberg's work before coming to Colorado.

All three of the self-organizing systems we have described, at three different levels of biological organization, should be clearly recognized to have many common features. In each case there is a freedom on the part of the system being organized to explore a variety of alternative states, and in each case the final end state attained by the system is "the" one which is energetically favored in some appropriate sense. The nature of the units and the forces between them are grossly different, but formally the phenomena are all the same.

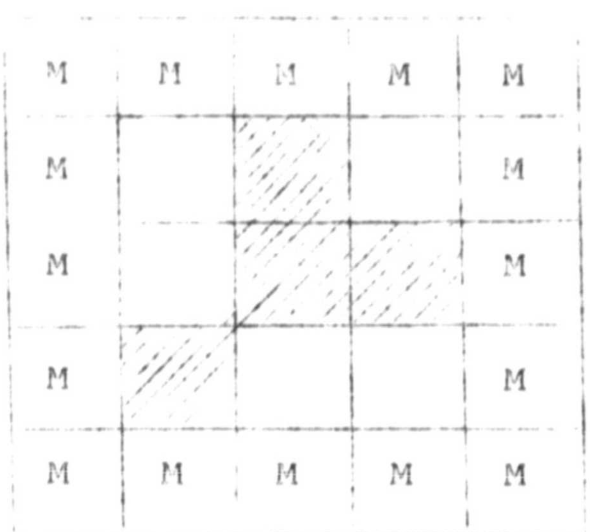
The problem around which I would like to organize this summer's work is the following: to determine the morphogenetic capabilities of systems of motile, cohesive units; particularly their capabilities to form structures of biological interest, such as tubules and lamellae. At our disposal are the adhesive or cohesive interactions between the units, and the measure of energy or potential which we impose on the system. What we wish to determine are such questions as: does a particular choice of interactions give rise to a single unique preferred end-state of least energy? Can we choose interactions in such a way that a particular desired end-state (e.g. a tubular structure) becomes a preferred end-state? If this can be done at all, can it be done in more than one way, can we devise experimental tests to distinguish between the alternatives? Do the values so determined throw any light on the nature of the underlying cohesive forces between the units (e.g., are they such that, say, van der Waals interactions are excluded)? If we cannot generate particular real biological patterns with differential adhesiveness and motility alone, can we introduce other organizational principles in a systematic way so that the desired patterns will be produced? Some examples: adhesions not constant but variable according to the enviornment of particular units; adhesions variable in time; differential cell multiplications and cell deaths permitted in the system. In each case the aim is to propose specific algorithms for the generation of biologically interesting structures, based only on the properties of the units comprising the system, together with some means of determining in experimental situations whether one or another possible algorithm is actually implemented in a specific case.

If we can do this with reasonable assumptions on the nature of the units, we shall have thrown light on morphogensis in differentiating systems as self-organizing systems. If we cannot do this, it follows that real morphogenesis is not entirely a process of self-organization, but that added information is coming in from outside. This is not entirely impossible; at the other biological levels mentioned earlier, it seems likely that the assembly of more complicated virus particles (e.g. the T-even bacteriophages) are not entirely self-assembly processes, and even that the folding up of polypeptide chains is enzymatically assisted in some cases. In either case, we will have learned something important about real morphogenesis, starting with the behavior of artificially produced cell populations.

To fix ideas, let me describe briefly a model that I have set up for the study of these problems. I do not intend that this model shall occupy us exclusively this summer; I only mention it to help fix ideas. By all means, feel free to pursue it if it seems germane to your own thoughts on the subject, but feel equally free to develop your own methods of approach.

Let us consider initially a population made up of two cell types, like Steinberg's mixture of heart and retinal cells, immersed in a medium. The model is two-dimensional for simplicity, but it generalizes easily to three dimensions, and to any number of cell types. We idealize the population as a (region of a) plane, divided up into squares, and thus forming a tesselation. At an instant of time, each square in the tesselation is occupied by a cell of one type or another (let's call them <u>black</u> and <u>white</u>) or by the medium, and the configuration is specified by numbering the squares in the tesselation in some convenient way and specifying what kind of cell occupies the square at the given instant. Each such configuration is called a pattern. For simplicity, we suppose that the number of cells of each type is fixed and does not change.

An example of such a pattern is shown in the next figure; black cells are hatched, white cells are vacant, and squares containing medium are indicated by an M:



Notice that there are five different kinds of edges which can occur in such a pattern. A black cell may abut against another black cell, against another white cell, or against a square containing medium. A white cell may abut against another white cell or against a square containing medium. We do not care about adjacent squares both containing medium. Thus the five different kinds of edges which occur in such a pattern may be denoted by:

BB, BW, BM, WW, WM

For any given pattern, we can count up the number of edges of each type in the pattern. In the above pattern, we have:

BB=2, BW=8, BM=4, WW=2, WM=8.

Let us now associate a number with each edge type ( ) which will measure the adhesiveness between the corresponding cells. For instance, let us choose:

F(BB)=2, F(BW)=0.5, B(BM)=0, F(WW)=1, F(WM)=0.25

For a given pattern, we can multiply the number of edges of each given type by the number representing the adhesiveness between the corresponding cells. Adding these together, gives us a measure of the <u>total energy</u> of the pattern. For the above pattern, with the above choice of adhesive strengths, we find the total energy E(P) is:

$$E(P) = 2.2 + (0.5).8 + 0.4 + 1.2 + (0.25).8 = 12$$

So much for pattern statics. We must now turn to the question of the way in which these patterns can change in time. There are a variety of different ways of doing this; the one I describe being typical. Let us say that two patterns P1, P2 differ by an elementary permutation if they are identical except that the contents of two adjacent cells are interchanged. Two elementary permutations are called compatible if they involve nonoverlapping pairs of squares of the tesselation. We shall say that two patterns are <u>neighboring</u> if they differ by a number of compatible elementary permutations. Thus, any individual pattern P0, determines a set of other patterns which are its <u>neighbors</u>. The neighbor relation between patterns is not transitive.

If we think of time as moving along a discrete set of instants, we have to say what P(t+1) will be when P(t) is given. Let us look at the pattern P(t) and the set of its neighbors. Evaluate the energy E of each neighbor, as described above. If there is a uniquely determined pattern with minimal energy, this is P(t+1). If not, we can use one of a variety of rules to specify, out of the subset of neighbors of P(t) with minimal energy E, a unique one which will then P(t+1). We continue this process until it eventually stops.

We can see, I hope, how to formulate all the queries mentioned earlier in terms of this model, having at our disposal (a) the number of cell types; (b) the number of cells of each type; (c) the adhesiveness per edge type. The model itself, however, is rather linear; the total energy E(P) of a pattern P being a scalar product of two vectors; thus we would expect limitations on the kinds of stable end patterns we could specify with such a model.

I hope that enough has been said to orient you toward the kind of problems we would like to consider this summer. I attach herewith a reading list with which I hope you will familiarize yourself, so that we can plunge right in.

READING LIST

On Protein Tertiary Structure.

1. Anfinsen, C. B., "Spontaneous Formation of 3-Dimensional Structure of Proteins" in The Emergence of Order in Developing Systems, M. Locke, editor. Academic Press, 1968.

On Virus Assembly.

1. Caspar, D. L. D. & Klug, A. "Physical Principles in the Construction of Regular Viruses." Cold Spring Harbor Symposia, XXVII, (1962), 1-24.

2. Caspar, D. L. D., "Assembly & Stability of the Tabacco Mosaic Virus Particle." Adv. Protein Chemistry, 18, (1963), 37-121.

3. Kellenberger, E., "Vegitative Bacteriophages and the Maturation of Virus Particles." Adv. Virus Research, 8, (1961), 1-61.

On Cell Sorting.

1. Steinberg, M. S., "Reconstruction of Tissues by Dissociated Cells". Science, 141 (1963), 401-408.

2. Steinbert, M. S., "The Problem of Adhesive Selectivity in Cellular Interactions.", Cellular Membrande and Development, M. Locke, editor, Academic Press, 1964.

See also the references by Holtfreter, Moscona, Townes, Weiss cited in Steinberg's bibliographies.

For comparison of Steinberg's models with another level of physical organization, you might look at Torza, S. and Mason, S. G., "Coalescence of Two Immiscrible Liquid Drops." Science, 163, (1968), 813-814.

PATTERN GENERATION AND MORPHOGENSIS

b) Report

Some consequencies of a hypothesis proposed by Steinberg on the self-sorting of cells are examined. The hypothesis proposes that two properties, motility and differential adhesion, are sufficient to account for cell sorting. The final configuration reached in pure cell sorting will be one in which the surface free energy of the system will be at a minimum. Immiscrible liquid drops are an analogue of such a system.

We examine the implications of this hypothesis for the morphorgenesis of real biological patterns. The system is here modeled as a two dimensional grid, whose squares represent cells or ambient medium. A contact edge between two cells is assigned a lambda value, which may be zero or positive. Lambda thus represents the "strength of adhesion." The sum of the products of contact edges, and their respective lambda values is E, which may be regarded as the negative of the total surface free energy of the system. Configurations are maximaly stable when E. is at a maximum. The constraints on the values of lambda which produce configurations with maxium E have been found for configurations of two and three cell types

The concept of neighboring configurations is introduced. A configuration is neighboring to another if it can be reached from it by cell motility in unit time, assuming certain plausible rules of cell motility. Then certain configurations are at local maxima of E, since neighboring configurations have lower E. values. Hence, once reached, they will be stable. A number of histologicaly interesting configurations are shown to be such local maxima. It is shown that configurations may be path dependent: i.e. can only be reached, given certain motility rules, from a restricted number of initial configurations.

SELF-REPRODUCING AUTOMATA, RELATIONAL SYSTEMS AND CELL THEORY

a) Proposed program - pre-circulated

A selection of papers covering the topic of relational systems was distributed.

SELF-REPROCUCING AUTOMATA, RELATIONAL SYSTEMS AND CELL THEORY

b) Report

Hierarchical Control Theory & Relational Systems in Biology.

Recognizing that hierarchical organization and control distinguishes living from lifeless matter, this group has pursued as its central problem, the logical and physical basis for the origin and propagation of hierarchical systems. A general definition of hierarchy was developed along with the specific concepts of hierarchical control and hierarchical control continuability. (Papers by Hamann and Bianchi, and Pattee are in preparation.) Numerous examples of hierarchical systems were discussed. A preliminary model for the autonomous emergence of life was developed which satisfied certain necessary conditions. The most crucial specific problem in these considerations was the identification and characterization of the stochastic stability necessary to maintain an hierarchical constraint.

In addition, the participants have made the following particular contributions toward various aspects of the problem of this group.

M. Pincus: Development of a probabilistic extremization method - relevant to the formal investigation of stochastic stability.

P. Bright: Discussion of precedence of stochastic vs. deterministic descriptions - relevant to hierarchical form.

R. Moore: Discussion of biological information (entropy); coded information - relevant to probabilistic hierarchical levels.

D. Shear: Paper on stability in chemical reactions - relevant via modified H-functions to stochastic stability studies.

S. Stivala: Outline of book on properties of macromolecules - relevant to characterization of molecular stability.

M. Conrad: Paper (thesis) on computer-simulated ecosystems - relevant to study of population stability and effect of enviornment on biosystem stability.

N70-18503

INFORMATION PROCESSING BY CELL ASSEMBLIES

a) Proposed program - pre-circulated

The program will consist of a series of lectures of which the following topics are a partial list:

I. Information Processing in Nerve Cells and Nerve Nets:

The response properties of single nerve cells.

Statistical aspects of information acquisition and processing.

Information processing in sensory pathways.

The significance of single cells and groups of cells in information processing.

Randomness and design in functional organization.

II. Mathematical Topics:

Dynamical Systems theory treatment of single cell responses and multi-cell interactions.

Mathematical theories of a psychophysical phenomenon (Binocular space perception).

Members of this study group may give other lectures in addition to those mentioned above.

There will be two specific research problems to which this group will address itself, but others may be added to the list later. Present plans are to investigate a specific nerve net i.e. the amacrine-bipolar net in the retina using the best information available on neural responses and interaction properties. The object of this work will be to obtain some insight into nerve interactions in general and in this particular instance one may hope to find out more about the relation of nerve net responses to a (behavoral) psychophysical phenomenon, such as visual adaptation.

The other problem concerns binocular space perception. Here again, one may be able to relate psychophysics to neural "machinery". For, there is a good deal of information from psychophysical experiments; there is a mathematical theory of binocular space perception (Luneberg); and recently there have been some related neurophysiological data on this problem (Barlow). There are certain neural net hypotheses which can be proposed and investigated.

INFORMATION PROCESSING BY CELL ASSEMBLIES

b) Report

The program for this group had to be organized, keeping in mind that a) it was too large to work on a single problem, b) that its members came from diverse backgrounds, c) that the resources of the members needed to be utilized in attacking the problems to be formulated.

It was therefore, decided to devote the first week or ten days to a series of seminars in which the individual group members would present accounts of their work and interests. This done, two research problems were presented to the group, one on visual adaptation and the other on binocular space perception. The first is at present under active investigation in a number of laboratories and regarding the second, there is an extensive mathematical theory which was formulated by Luneberg some 20 years ago on the basis of psychophysical data and now some neurophysiological data have become available, which have a bearing on the problem.

In the adaptation problem we are concerned with the relationship of psychophysical data to the responses of single cells and cell assemblies, primarily in the retina. In the space perception problem the relationship is between psychophysics, the geometry of the eyes and information processing which is presumed to take place in the visual cortex.

The following work was done on the adaptation problem:

1. A neural model was proposed, based on experimental

evidence, which reconciles some apparently paradoxical data and which should account for the major adaptation phenomena.

2. A quantitative comparison has been carried out of some stimulus parameters and the corresponding responses in behavioral experiments with data relevant to receptive field organization.

3. Empirical curve fitting was carried out to determine the input-output relations in the various neurons in the retina, with a view to synthesizing an appropriate nerve net and simulating quantitatively adaptation phenomena.

The following work was done on the space perception problem:

1. A model was proposed relating behavioral data to a neural hypothesis of binocular space perception.

2. Preliminary calculations indicated that our model would lead to different predictions from the Luneberg theory and since there were insufficient data to test our theory, we set up some simple experiments in which most of the group served as subjects. Our results so far had been encouraging.

3. Then we obtained a book through the inter-library loan service, which had been difficult to find and obtain, and in which Blank had made some modifications to the Luneberg theory and confirmed them on a series of experimental results. We did some calculations which showed that our neural hypothesis could be reduced formally to Blank's theoretical treatment. Although this means that the results of our theory had to some extent been anticipated, it also implies that we can have confidence in our neural hypothesis.

Our contribution to date, therefore, consists of our experimental data and the neural model of binocular space perception with all its possible implications.

Neither the work on adaptation nor on space perception is at a stage of completion. This is hardly to be expected in so short a time. However, the work has advanced sufficiently to be able to say that some very interesting possibilities have been opened which need to be pursued and brought to a conclusion.

We are preparing progress reports to take with us, so that we can continue this work and we hope to keep in touch at least until this work is done.

BUDGET

Attendees:

1	Director
9	Faculty Members
30	Students
56	Dependents
96	Total Attendance

Honoraria:			
Faculty and Director	9,600.00		
Support Staff	1,530.00		
Students	6,500.00		
			17,630.00
Subsistence:			
Director, Faculty and Dependents	4,413.57		
Support Staff and Dependents	1,677.79		
Students & Dependents	8,072.75		
			14,164.11
Travel:			
Director, Students, and Support Staff	5,722.20		
			5,722.20
Miscellaneous:			
Telephone	200.00	(estimate)	
Braiden Office Rental	175.00		
Rental of Xerox	275.00	(estimate)	
Paper, Office Supplies	125.00	(estimate)	
Petty Cash	66.35		
Secretary	450.00	(estimate)	
Equipment Rental	100.00	(estimate)	
Computer Needs	250.00	(estimate)	
Books	217.25		
Student Facilities Charge (30 @ 12.50)	375.00		
			2,233.60

TOTAL 39,749.91

NAME	BOARD AND LODGING	TRAVEL	HONORARIUM
James F. Danielli	679.96	174.30	1,200
Brian Goodwin	150.60	674.70	1,200
Howard Pattee	769.14	132.30	1,200
K. N. Leibovic	681.88	174.30	1,200
Paul Schaie	508.86	180.40	1,200
Robert Rosen	722.23	174.30	1,200
M. Ycas	237.03	197.40	1,200
J. Hamann	166.95	174.30	600
L. Bianchi	450.80	174.30	600
H. Pollard	98.12	130.60	none
H. Collins	905.05	174.30	765
M. May	772.74	174.30	765
Arthur Winfree	333.90	200.00	400
Stuart Kaufman	333.90	147.00	400
Edward Manougian	391.39	200.00	400
Warren Woolley	166.95	139.00	300
Karen Moelling	166.95	132.30	300
Narenda Goel	431.12	none	400
Richard Campbell	450.80	132.30	400
Lloyd Demetrius	135.24	132.30	400
Hugo Martinez	502.85	132.30	400
Michael Conrad	333.90	none	300
Richard Moore	166.95	200.00	400
Peter Bright	166.95	174.30	400
Martin Pincus	333.90	200.00	400
David Shear	529.85	195.30	400
Erik Balslev	337.24	174.30	400
Kenneth Reid	528.05	200.00	400
Kwang Jeon	579.80	174.30	400
Herbert Geller	333.90	153.30	none
Clara Torda	225.40	200.00	"
O. Dayle Sitler	166.95	none	"
Thomas Mathieson	166.95	"	"
G. Pertile	170.47	"	"
V. Jayanthinathan	166.95	"	"
S. Newman	337.24	"	"
D. Mantik	166.95	"	"
S. Stivala	100.17	"	"
Mrs. V. Jordan	166.95	"	"
Dr. Gordon	16.46	200.00	"
Francis Young	169.62	none	"
Richard Schwartz	(Student Facilities Charge Only)		
Paul Cull	"	" "	"
	14,164.11	5,722.20	17,630

APPENDIX I

Material used for recruitment of personnel

Center for Theoretical Biology
4248 Ridge Lea Road
State University of New York at
Buffalo
Amherst, N.Y. 14226

Dear

In reply to your inquiry concerning the Colloquium on Theoretical Biology which is to be held at Colorado State University at Fort Collins from July 13 to August 15;

A copy of the original leaflet concerning this colloquium is enclosed herewith, listing the topics to be considered.

The colloquium will consist of formal meetings for five days a week. There will be one formal lecture daily at 8:30 a.m., attended by all members of the colloquium. After discussion of this lecture, individual working parties will assemble and work through until lunch time, probably 11:30 a.m. After lunch there will be a recess until early evening to enable members to take advantage of the recreational facilities available. These are excellent. The working parties will meet again during the evenings.

The agenda of each working party will be set up by discussion between the working party leader and the members of the working party.

Those wishing to attend will be admitted primarily with a view to their participation as a working member of one of the working parties. Facilities will be provided for other spontaneous working parties, should this be required.

It is anticipated that many of those attending the colloquium will wish to bring their families with them. Some members of the colloquium will receive meals and room accommodation free of charge. Pre-doctoral members will receive an honorarium of $75 per week and post-doctoral members will receive an honorarium of $100 per week. Tourist air fare for members of the symposium will be paid, with an upper limit of $200 for the round trip. Those members of the symposium who prefer to travel by car may receive a travel allowance equivalent to the tourist round trip air fare, but again with an upper limit of $200.

Travel expenses cannot be provided for members of the families of participants, but accommodation and meals will be provided for up to three dependents.

Admissions to membership of the colloquium will be announced approximately March 21. Enclosed is an application form which should be returned to us at the earliest possible moment. Please do not fail to attach the statement requested on point 12 of the form, indicating your reason for wishing to attend the colloquium and, in particular, with which working party your primary interest will lie.

All members of the colloquium are expected to be present throughout the colloquium. Please do not apply unless you are sure that you can meet this condition.

Yours sincerely,

JFD:vip
Encs.

James F. Danielli

THEORETICAL BIOLOGY COLLOQUIUM

A colloquium on the Theoretical Biology of the Cell will be held at Colorado State University under the administration of the American Institute of Biological Sciences from July 13 to August 15, 1969. The program is sponsored by the National Aeronautics & Space Administration. It is designed to stimulate and encourage active research in theoretical areas related to the cell and in particular, systems theory studies. The course of study will include lectures and seminars, but emphasis will be placed on encouraging participants to take part in one of several working parties, details of which are given below. Facilities may also be provided for working parties in other areas. Both pre- and post-doctoral fellowships are available for those wishing to attend. Accommodation in the University is available to those attending and their families. The working parties and the faculty member primarily responsible are indicated below.

1. Time-dependent variation in cells - B. Goodwin
2. Intracellular relationships and cell reassembly - E. Pollard, J. F. Danielli
3. Morphogenesis and pattern generation - R. Rosen, M. Ycas
4. Self-reproducing automata - H. Pattee
5. Information processing by cell assemblies - K.N. Leibovic
6. Relational systems and cell theory - J. Hamann, L. Bianchi

Those desiring further information should write to the Director of the Institute:

Dr. J. F. Danielli
Center for Theoretical Biology
Summer Colloquium
4248 Ridge Lea Road
State University of New York at Buffalo
Amherst, New York 14226

The closing date for receiving applications is February 1, 1969.

APPLICATION FOR SUMMER COLLOQUIUM IN THEORETICAL BIOLOGY

Indicate in this box which working parties you wish to work with in sequence of preference.

1. Name: ______________________________
2. Address: ______________________________

   ____
3. Age.______ Married____ Single _____ Spouse 1st name ______________
4. Present Position: ______________________________
5. Education:

   Institution | Dates | Degrees

6. Employment:

   Employer | Dates | Nature of Work

7. Citizenship:__________
8. Main field of interest:______________________________
9. Five most important publications relevant to the Summer School:

10. Name and address of three referees:

    ____

    ____

    ____
11. Number of dependents who will accompany you: Children ________
12. Attach a one-page statement indicating your reason for wishing to attend this program.

March 14, 1969

Dear Dr. ____________:

The Selection Committee for the Theoretical Biology Colloquium this summer has asked me to say that you have been accepted for study group # ______ on ______ ____________________ for which the faculty members are ______________________. We shall be able to provide free room and board for yourself and ____________ dependents. We shall also be able to provide an honorarium of $_____________. Irrespective of your method of travel, return tourist airfare for one person will be available, with an upper limit of $200, from your home to Denver, which is the nearest airport to Fort Collins.

If you join the Colloquium, it will be necessary for you to arrive in Fort Collins not later than Sunday, July 13. You will be able to leave on Saturday, August 16. On Monday, July 14, the study groups will meet for final discussion of the working program, and on Tuesday, July 15, there will be a formal presentation of these programs to the Colloquium as a whole. At that time it will be possible for you to change your study group, or to arrange to participate in the affairs of more than one study group, should this appear to be desirable.

There are two points which I should emphasize to avoid any misunderstanding. The first is that this invitation to participate in the Colloquium is on the supposition that you will be present for the full period of the Colloquium, i.e., will not leave before Saturday, August 16, and will take off only those days during this period which have been set aside by the faculty for recreation. The second point is that if you are bringing children with you, it must be on the understanding that adequate supervision will be provided by parents, either individually or by group arrangements. I must emphasize this because at one of our previous meetings failure to supervise children led to much damage being done to University property. I am sure you will forgive me if I emphasize that if the children are not properly supervised, we shall be obliged to ask the family concerned to find accommodations away from the Fort Collins campus.

This conference is being made available through funds provided by NASA and administered by A.I.B.S. However, because of financial stringency, the money available for this Colloquium is less than has been the case in the past. We have encountered a considerable rise in living costs at Fort Collins, and there has recently been a rise in air fares. Consequently, we have been unable to invite as many individuals to attend the Colloquium as we would have wished. If therefore you are in a position to pay for your travel, or board and lodging from other sources such as research grant, please let me know at the earliest possible moment. The funds thereby released will be used to enable others to attend the meeting. A number of contributions of this nature have already been made, and I assure you such contribution will be deeply appreciated.

Please acknowledge receipt of this letter, and return the enclosed form at the earliest possible date.

I look forward with the greatest pleasure to seeing you in Fort Collins. With best wishes.

Yours sincerely,

James F. Danielli

JFD/lg
Enc.

STATE UNIVERSITY OF NEW YORK AT BUFFALO

Health Sciences Center

CENTER FOR THEORETICAL BIOLOGY

4248 RIDGE LEA ROAD
AMHERST, NEW YORK 142

April 11, 1969

Dear

We regret to inform you, that much as we would like to have you participate in the Summer Colloquium, in Theoretical Biology, we are unfortunately unable to do so, due to the shortage of funds. Your name will be placed on the reserve list, in the event that a cancellation occurs. If you can find funds to enable you to participate we will be most happy to make arrangements for you to join a working party.

Thank you for your interest. Your name will be placed on our mailing list for future colloquia. With best wishes.

Sincerely yours,

Marian May

Marian May

STATE UNIVERSITY OF NEW YORK AT BUFFALO

Health Sciences Center

NTER FOR THEORETICAL BIOLOGY

4248 RIDGE LEA ROAD
AMHERST, NEW YORK 14226

April 11, 1969

Dear

The selection committee for the summer colloquium in Theoretical Biology has asked me to say that your application was not accepted, since in view of the way the program for the colloquium has developed, you would not be able to effectively participate in it. We thank you for your interest in this colloquium and will mail to you details of future colloquia.

Sincerely yours,

Marian May

SAMPLE LETTER TO THOSE APPLYING LATE

Dear _______________:

Thank you for your letter. We deeply regret that we have already allocated finances for the 1969 Theoretical Biology Colloquium. We could only consider applicants now for people who are self sustaining.

With best wishes,

NOTES ON ORGANIZATION AND CHECK LIST

for future colloquia.

I. Advance planning

II. Operations at CSU, Fort Collins, Colorado

III. Recommendations

IV. Check List

I. The summer colloquium for Theoretical Biology began with applications from prospective attendees. Three brief references were requested for each applicant. An ad hoc committee and all the faculty members together with the director met in New York City for the purpose of selecting from the applicants, those to be invited.

After the invited had replied in acceptance, all correspondence from this point onward was done between the assistant to the director, under his supervision, and the attendees who were expected to attend.

The correspondence covered:

a. Names, ages and sex of those to accompany each attendee

b. Any special request

c. Understandings between CSU and AIBS

d. Rules and regulations governing medical services at Colorado State University.

e. Room assignments

f. Maps and instructions for travel

g. Lecture timetable and faculty agenda

h. Preliminary reading list

i. Date and time which participants were expected to arrive and leave

During the faculty and ad hoc committee meeting, faculty members were asked to send their requests for books they wished to have ordered, atom models needed for lectures and computer facilities they wished to have available during the conference. The library set up in 1966, was itemised and sent in advance to CSU, where it was organized as the colloquium library. At the end of the colloquium, it was returned to the Center for Theoretical Biology. These orders were made prior the starting date and all deliveries were made to CSU.

II. Upon arrival at CSU, each family checked in at the dormitory desk and were issued the following:

1. Room keys
2. Meal tickets
3. Folio (containing additional information)

A meeting for all attendees and families and CSU staff was held the first week to give everyone an opportunity to become acquainted, with facilities.

General lectures were held two or three mornings a week from 8:30 to about 10:00. Working parties then went to their own meeting rooms until 11:30, lunch time. Families were free to do as they wished from this point until 7:00 p.m., when evening meetings were held Monday through Thursday. The stopping time of these sessions depended on the progress of the groups. Much of the time participants were involved until after 10:00 p.m. Some working parties had special afternoon discussion sessions of general interest to the colloquium.

Near the close of the sessions, CSU figured the charges for each family. Any charges for which AIBS was not responsible were collected by the CSU staff during the colloquium.

On the last day, each person or family in attendance, was responsible for returning room keys to the dormitory office when checking out.

III. Comments on the colloquium arrangements for the dependents.

The letter sent to participants requesting that parents provide adequate supervision for their children, resulted in a very troublefree colloquium. No complaints regarding the behavior of the children were received.

The colloquium this time was very unstructured, and groups formed spontaneously for such events as picnics, games, trip to the mountains, etc. Organization of the families was found to be undesirable in this instance and overall group interactions were satisfactory.

Due to the limited budget available, it was found necessary to have parents of one child under five years old, share a room with the child. This was not a very satisfactory arrangement, and some solution should be considered for the next colloquium.

IV. Check List.

a. Appoint faculty members.

b. Publish and circulate notices and ask for those interested to request applications.

c. Send out application blanks.

d. Check application forms after they are returned.

IV. Check List. (continued)

e. Open file on each applicant.

f. Send out reference forms.

g. Select ad hoc committee to work with faculty members for screening applicants.

h. Set date for committee meeting for selecting attendees.

i. Send letter inviting those who have been selected and ask them to respond if they accept.

j. Send letter to participants concerning recommendations (1-4) page 50 of this report.

k. Cover correspondence procedure in same manner as in Part I, page 50 of this report.

l. Send letters of regret to unsuccessful candidates.